Necessity of a loading dose when using vancomycin in critically ill patients

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Sir,

We are interested in the question of the need for a loading dose in critically ill patients receiving vancomycin. Soto et al. found that standard vancomycin doses of 500 mg (7.5 mg/kg) every 6 h are subtherapeutic in critically ill patients during the first 24–48 h. Since vancomycin is a concentration-independent antibiotic with time above the antimicrobial MIC being the best predictor of efficacy, Ackerman et al. emphasized the need for maintaining trough concentrations ≥8 mg/L if adequate antimicrobial efficacy is to be ensured. Excessive peak concentrations should nevertheless be avoided to minimize toxicity. An ideal vancomycin loading regimen should facilitate the achievement of drug levels ≥8 mg/L throughout the first 24–48 h, while avoiding toxic peak levels. Although loading doses between 20 and 30 mg/kg have been proposed to serve these purposes, the safety and adequacy of these regimens in critically ill patients have not yet been prospectively studied.

A recently completed study at our institution provided useful information on the above-stated question. The study was aimed originally at evaluating the bioequivalence of generic and brand-name vancomycins. Patients with sepsis due to serious Staphylococcus aureus infections were randomized to receive vancomycin with a 25 mg/kg loading dose infused at a rate of 500 mg/h followed by maintenance doses adjusted for renal function. Twenty-eight patients, of whom 25 had methicillin-resistant S. aureus (MRSA) bacteremia, two had methicillin-susceptible S. aureus bacteremia and one had MRSA lung abscess, were enrolled to receive the above regimen and had 1 h post-loading concentrations determined. All of the S. aureus isolates had vancomycin MICs = 2 mg/L. We then re-analysed the data of all 28 patients as a group to find the range of post-loading vancomycin concentrations after the 25 mg/kg loading dose. The average 1 h post-loading serum vancomycin concentration of the 28 patients was 26.4 ± 9.3 mg/L (mean ± s.d.), determined by commercial fluorescence polarization immunoassays (TDx, Abbott Diagnostics, Irving, TX, USA). None of these patients developed adverse events, such as red man syndrome, hypotension, tinnitus or hearing impairment, during infusion of the loading dose.

Our data showed that a 25 mg/kg loading dose of vancomycin infused at a rate of 500 mg/h is safe in critically ill patients, without producing toxic peak levels. By providing 1 h post-loading serum concentration in the range 26.4 ± 9.3 mg/L, it accelerates the build-up of trough serum vancomycin concentrations above 8 mg/L throughout the first 24–48 h to ensure the best possible therapeutic outcome.

References


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